Gustatory Effectiveness and Acceptability of Fluoroacetate Derivatives in Rats

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21. フッ化酢酸塩のネズミに対する味覚効果ならびに摂取性について

草野忠治（鳥取大学農学部） 51. 3. 16 受理

ネズミでの1080, 1081の摂取性が味覚生理学的方法により調査された．1081は1080よりも摂取性が良好であった．これは両者の鼓索神経を介しての味覚効果の差異よりも，むしろ毒作用の速度の差異に関係づけられる可能性が強い．ニッソールはネズミの鼓索神経をなんら発火させなかった．

After the Second World War, the chemical control for rats and voles in agricultural area in Japan has been extensively carried out with sodium monofluoroacetate (1080), of which has not only the merits of the rapid toxic action and the high control efficiency but also the demerits of strong toxicity and hazard of secondary poisoning to non-target animals. Possible causes responding to high control efficiency of 1080 against rodents have not been analyzed by a physiological method as yet. Fluoroacetamide was lower toxic to rodents than 1080 and was first suggested as a potential rodenticide by Chapman and Phillips[1]. This poison has not been still registered as a rodenticide in Japan.

In the present paper, the gustatory effectiveness of fluoroacetate derivatives and their acceptability in rats were analyzed from both the behavioral responses and the electrical responses of the gustatory nerve to these poisons.

Materials and Methods

Male adult rats of Wistar strain, weighing 150-250g were used.

The candidate toxic compounds were sodium monofluoroacetate (1080), fluoroacetamide (1081) and Nissol [N-methyl-N-(1-naphthyl) monofluoroacetamide]. Also sodium chloride and sodium acetate were used as standard gustation substances.

1. Acceptability thresholds

Three kinds of thresholds-the taste threshold, the threshold for discrimination, and the absolute rejection threshold-of 1080, 1081, sodium chloride, and sodium acetate were determined by the two-bottle preference method as reported in our previous paper[2]. Each starting concentration of 1080, 1081, and two sodium salts was 0.000001, 0.0002, and 0.000002 per cent respectively.

2. Acceptability and toxicity of 1080 and 1081

The preference of albino rats to the plain water and the poison solution of various concentrations, which were about or beyond the concentration necessary to the occurrence of the toxic effect of 1080 and 1081, was carried out by the same method as described in our previous paper[3]. After 24 hours, the amount of intake of both the poison solution and distilled water was determined. This method was defined as the direct two-bottle preference test. Afterwards the mortality of the rats was observed for seven days.

3. Gustatory nerve response

Integrated responses of the whole chorda tympani nerve to 1080, 1081, Nissol, sodium chloride and sodium acetate applied to the tongue surface of the rat were recorded by a platinum wire electrode (100μ in diameter). The exposure of the whole chorda tympani nerve and the recording method of nerve response were similar to those described in our previous report[2].

Results

Acceptability thresholds

More of the solution of 1080 than the plain water was accepted at lower concentrations and the amount of intake of both the test solution and the plain water decreased together with the increase of the concentration of 1080 beyond the concentration of 0.0002 to 0.001 per cent. All the rats had died at the concentrations from 0.008 to 0.13 per cent without the discrimination between the poison solution and the plain water (Fig. 1). The daily intake curves of 1081 were similar to those of 1080. Namely, the amount of intake of both the solution of 1081 and the plain water lowered together at

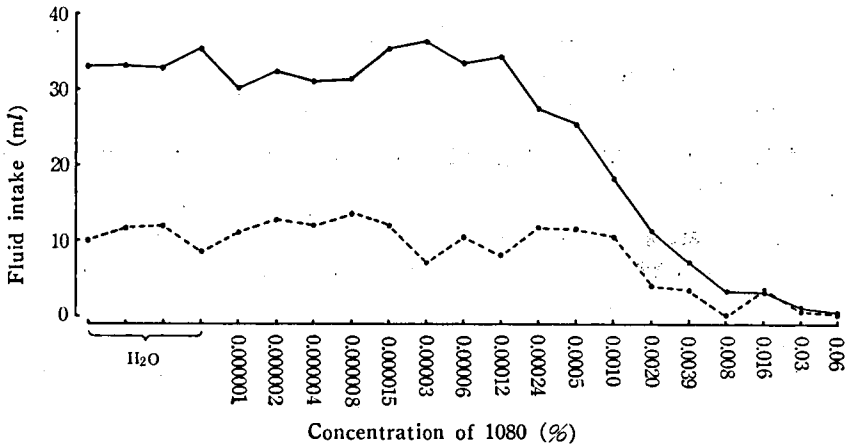

Fig. 1. Averaged daily intake curves for five rats on 1080.
—•—: 1080, --•--: distilled water.

the concentrations from 0.008 to 0.016 per cent and these were scarcely taken at the higher concentrations from 0.02 to 0.05 per cent without the discrimination. The mortality for 1080 was 5/5, whereas that for 1081 was 2/5.

The acceptability of sodium chloride and sodium acetate was determined by the same method as described in above experiment. These salts were pleasantly accepted with the increase of the concentration under the maximum acceptance concentration, whereas beyond this concentration these salts were markedly rejected with the increase of the concentration (Table 1).

Acceptability and toxicity of 1080 and 1081

The results were given in Table 2. In the case of 1080, the poison solution at from 0.002 to 0.008 per cent was accepted more than the plain water and the majority of test rats did not die. Beyond the concentration of 0.008 per cent, the plain water was accepted more than the poison solution and the mortality had tended to increase with the increase of the concentration of the poison. On the contrary, the solutions of 1081 at higher concentrations from 0.06 to 0.48 per cent than those of 1080 was preferred more than the plain water and the majority of test rats died. Total volume of both the poison solution and the plain water which were drunk at the concentration of 0.002 per cent of 1080 decreased to about 60 per cent of normal level and beyond the concentration of 0.002 per cent it decreased markedly with the increase of the concentration of the poison. In the case of 1081, the decrease of total amount of intake of both the poison solution and the plain water was less than that in 1080.

Response of gustatory nerve

When one ml of 1080 at the concentration from 0.06 to 1 per cent was applied to the tongue surface of the rat, a definite response was recorded from the whole chorda tympani nerve and the magnitude of the response increased with the increase of the concentration of the poison (Fig. 2). In the case of sodium chloride and sodium acetate, the whole chorda tympani nerve

Table 1. Acceptability thresholds of sodium chloride and sodium acetate in albino rats.

Test compound	Threshold for discrimination (%)	Maximum acceptance concentration (%)	Absolute rejection concentration (%)
NaCl	0.23±0.22	0.94±0.32	2.25±1.56
CH_3COONa	0.13±0.09	0.69±0.57	2.70±0.63

Body weight of albino rats: 200-250g. Tested rats in each group: 10.

Table 2. Direct two-bottle preference test with 1080 and 1081 in albino rats.

Test compound	Concentration (%)	Averaged amount of intake (ml) Plain water	Poisoned water	Ingested dose mg/kg	Ratio of ingested amount* (%)	Preference response P**>W***	P=W	P<W	Mortality	Survival (Days)
1080	0.06	2.4±1.5+	2.4±0.8+	5.9±2.2+	14±7+	2	0	3	4/5	1-2
	0.03	4.0±2.4	4.1±4.2	2.3±0.6	20±11	3	0	2	3/5	2-3
	0.015	4.5±4.0	12.6±11.2	8.2±7.4	42±28	3	0	2	3/5	1
	0.008	7.0±6.4	6.5±2.7	2.2±0.9	36±12	3	1	1	1/5	2
	0.004	6.5±3.7	7.9±1.4	1.4±0.2	41±11	4	0	1	0/5	
	0.002	8.0±4.2	16.0±2.5	1.4±0.2	58±8	4	1	0	0/5	
1081	0.48	2.7±2.9	6.4±3.0	122±49	25±7	4	0	1	5/5	1-2
	0.24	7.8±7.4	10.2±7.2	93±54	50±34	4	0	1	4/5	2-3
	0.12	4.6±3.4	5.7±1.7	28±5	31±7	3	0	2	4/5	1-5
	0.06	5.7±2.9	13.2±6.6	37±19	56±6	4	0	1	3/5	3-5

*: $\frac{\text{Ingested amount of poisoned water and plain water}}{\text{Ingested amount of plain water per day during predrinking test}} \times 100$,

: Poisoned water, *: Plain water, +:mean±S. D., Body weight of albino rats: 205-320g.

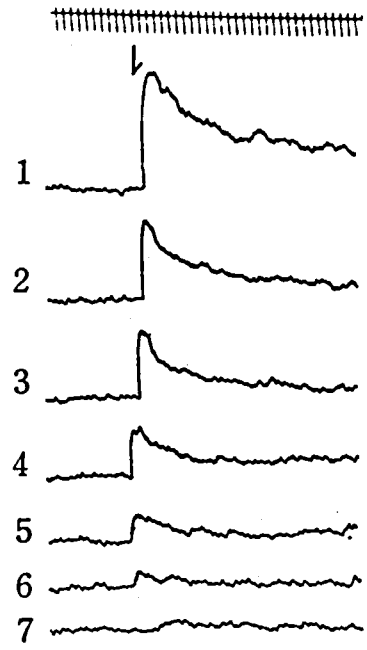

Fig. 2. Integrated responses of the whole chorda tympani nerve to 1080 and 1081.
1: 0.1M 1080, 2: 0.05M 1080, 3: 0.025 M 1080, 4: 0.0125M 1080, 5: 0.0063M 1080, 6: 0.0031M 1080, 7: 0.1M 1081. Time is in seconds.

had responded to these salts through the gustatory receptors on the tongue. The relationship between the concentration and the magnitude of

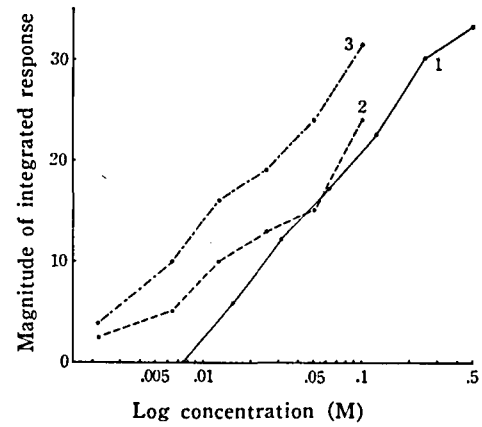

Fig. 3. Relationship between magnitude of response of the whole chorda tympani nerve and concentration in 1080, sodium chloride and sodium acetate.
1 : sodium chloride, 2 : 1080,
3 : sodium acetate.

the response of the gustatory nerve in 1080, sodium chloride, and sodium acetate was presented in Fig. 3. The gustatory effectiveness of sodium acetate was slightly larger than that of sodium chloride. The gustatory effectiveness of 1080 was approximately between each effectiveness of these salts. The gustatory effectiveness of 1081 for the whole chorda tympani nerve was very weak and such gustatory effectiveness in Nissol was not entirely observed.

Discussion

The daily intake curves of 1080, that Richter[4] obtained by the two-bottle preference test with Norway rats, were similar to those in the present experiment. The concentration at which the rats began to drink less of both the solution of 1080 and the plain water was defined as the toxic symptom threshold by Richter[4] and ranged from 0.0002 to 0.005 per cent. This result also was consistent with that in the present experiment. The daily intake curves of 1081 were similar to those of 1080 but the toxic symptom threshold of the former was several times higher than that of the latter. These results suggest that these two poisons did not give any unpleasant gustatory effectiveness against the rats and the occurrence of poisoned death during the two-bottle preference test might be brought from a chronic toxicity. Also, in the direct two-bottle preference test the solution of 1080 in the concentrations in about the toxic symptom threshold and over was accepted less than the plain water but higher mortality was obtained. In the case of 1081, the poison solution in the concentrations over the toxic symptom threshold was accepted more than the plain water and high mortality was obtained. Accordingly, the acceptability of 1081 is higher than that of 1080. Since the oral acute LD_{50}s of 1080 and 1081 in albino rats are 3.8mg/kg[5] and 13-15mg/kg[6,7] respectively, 1080 is more toxic to albino rats than 1081. As described later, the speed of the toxic action of 1080 was more rapid than that of 1081. Therefore, it is clear that there is the reverse relation between the magnitude of toxicity and the acceptability or the speed of the toxic action and the latter in these two poisons.

It has been advocated from the data of the electrophysiological responses of both the chorda tympani nerve of rats and the glossopharyngeal nerve of frogs that cations play an important role in the taste quality of inorganic salt solution and anions exert only a supplementary role[8,9]. In the present experiment, 1080, sodium chloride, and sodium acetate showed about the same order of gustatory effectiveness to the whole chorda tympani nerve of rats and the solution of lower concentration of these compounds was accepted favorably to the rats. Therefore, it is claimed that these compounds have such pleasant gustatory quality to rats as salt and this quality is mainly caused by sodium ions, although 1080 is tasteless in human beings from the paper of Richter[4].

Bentley and Greaves[7] showed that the time beginning to hesitate the continued feeding of the plain bait after the ingestion of a lethal dose of 1080 and 1081 with Norway rats was longer in the case of 1081 poisoning than in the case of 1080 poisoning. This result indicates a difference of the speed of the toxic action between 1080 and 1081. In the present experiment, the gustatory effectiveness of 1081 on the whole chorda tympani nerve of the rats was very hardly detected. In our unpublished data[10] with Norway rats, a preference test with the plain bait and the 0.3% 1080 bait, of which the base of these baits was wheat grain, showed that five out eight rats preferred the 1080 bait to the plain bait, the amount of intake of 1080 bait in the rats ranged from 0.20 to 1.27g (mean ; the poisoned bait 0.58 ± 0.03g per rat, the pure poison 1.73 ± 0.94mg/rat) and the mortality was 100 per cent. Accordingly, it was obvious that Norway rats fed the poison beyond the lethal dose, though the intake of the poisoned bait was a little. Further, the results with the Osaka University type Skinner-Box indicated that the acceptability of 1080 bait was low, though the mortality was 100 per cent[11]. Therefore, an amount of intake of 1080 bait is possibly limited by the rapid speed of the toxic action. Finally, 1081 may be markedly expected as an potent rodenticide, as Chapman and Phillips[1] pointed out.

Summary

1. The good acceptability of 1080, 1081, sodium chloride and sodium acetate in albino rats was showed by the two-bottle preference method. The rats died without discrimination between the solution of 1080 or 1081 and the plain water with the increase of the concentration of the poisons. Both sodium chloride and sodium acetate was markedly rejected in the concentrations beyond the maximum acceptance concentration.

2. In the direct two-bottle preference test the solution of 1080 in the concentrations of about the toxic symptom threshold and over was less acceptable to albino rats than the solution of 1081.

3. Three compounds, 1080, sodium chloride and sodium acetate, gave a definite gustatory effectiveness to albino rats through the whole chorda tympani nerve. The magnitude of gustatory nerve responce of 1080 was approximately between each effectiveness of these inorganic salts. The gustatory effectiveness of 1081 on the whole chorda tympani nerve was very weak and in Nissol it was not wholly observed.

4. Merits and demerits of 1080 and 1081 as a potent rodenticide were discussed.

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References

1) Chapman, C. and M. A. Phillips: *J. Sci. Food Agr.*, 6, 231 (1955).
2) Kusano, T., Y. Kasahara and Y. Kawamura: *Appl. Ent. Zool.*, 6, 40 (1971).
3) Kusano, T., Y. Kasahara and Y. Kawamura: *Appl. Ent. Zool.*, 10, 19 (1975).
4) Richter, C. P.: *J. Comp. Physiol. Psychol.*, 43, 358 (1950).
5) Barnett, S. A. and M. M. Spencer: *J. Hyg.*, Camb., 47, 426 (1949).
6) Phillips, M. A. and A. N. Worden: *Lancet*, 271, 731 (1956).
7) Bentley, E. W. and J. H. Greaves: *J. Hyg.*, Camb., 58, 125 (1960).
8) Beidler, L. M.: *J. Neurophysiol.*, 16, 595 (1953).
9) Sato, M.: *Science*, Japan, 29, 124 (1959) (in Japanese).
10) Kusano, T.: Unpublished data. (1965).
11) Kusano, T.: *J. Fac. Agr. Tottori Univ.*, 10, 15 (1975).